administration of aminophylline. Investigation of the arrhythmogenic effects of aminophylline given during halothane anesthesia in animals has shown that doses that produce blood levels corresponding to the therapeutic, nonarrhythmogenic range in conscious humans (10 to 20 mg per liter) are likewise not arrhythmogenic in animals. However, studies of the effect of higher, toxic doses of aminophylline (producing levels in the blood above 20 mg per liter) administered to animals during halothane anesthesia have shown that these high levels (which repeatedly have been shown to cause severe cardiac arrhythmias in conscious humans) are, in fact, arrhythmogenic in anesthetized animals.

In recent years, there have been reports of ventricular arrhythmias occurring in patients during halothane anesthesia following preoperative administration of aminophylline. Studies have been done in animals of the arrhythmogenic effects of aminophylline administered before anesthesia induction. Results have shown that even at theophylline levels in the blood that are considered safe in humans, ventricular arrhythmias frequently occur in the animals following induction of halothane anesthesia. In contrast, induction of enflurane anesthesia in animals appears safe even after toxic doses of aminophylline have been given.

On the basis of available information, the following guidelines are suggested for perioperative administration of aminophylline in humans. First, aminophylline given intravenously during halothane anesthesia in doses that produce accepted therapeutic levels (10 to 20 mg per liter) in the blood is unlikely to cause cardiac arrhythmias. A safe dose that is likely to produce such a level is 5 mg per kg of body weight for a patient who has not received aminophylline in the previous 24 hours (1 mg of aminophylline per kg of body weight will produce a 2 mg per kg of body weight rise in blood level). The drug should be diluted in 50 ml of sterile fluid and administered only by way of a peripheral intravenous route over five minutes. *Aminophylline given by way of a central venous line or pulmonary artery catheter often results in sudden death.*

Second, if aminophylline has been administered preoperatively, induction of halothane anesthesia may produce severe ventricular arrhythmias, even with circulating theophylline levels normally considered therapeutic and safe in conscious patients. Enflurane anesthesia used after preoperative administration of aminophylline, however, appears safe and unlikely to precipitate cardiac arrhythmias.

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Butorphanol and Nalbuphine: Two New Potent Analgesic Agents

TWO NEW ANALGESIC DRUGS have been released recently for the treatment of moderate to severe pain. Like pentazocine, these two drugs have mixed agonist-antagonist properties, which, it is hoped, will produce the *perfect balance* of analgesia without psychological or physiological effects.

Butorphanol tartrate, chemically related to levorphanol tartrate, is available in a 1 to 2 mg per ml solution; on a milligram basis, it has 3½ to 7 times the potency of morphine. Following intramuscular administration, it is rapidly absorbed, achieving a peak plasma level in 30 to 60 minutes, with a half-life of three hours.

In equianalgesic doses, respiration is depressed similarly with morphine or butorphanol. Interestingly, an increase in dose of butorphanol reportedly increases the duration, but not the degree, of respiratory depression. The hemodynamic effects of butorphanol resemble those of pentazocine, causing an increase in pulmonary artery and right atrial pressure with a decrease in cardiac output. However, the unpleasant psychotomimetic side effects reported with pentazocine occur only rarely with butorphanol. Euphoria does not result from butorphanol administration, and its addiction potential is judged to be low.

Nalbuphine, chemically related to oxymorphone and naloxone, is available in a 10 mg per ml solution; on a milligram basis it is variably reported to be equal to, or a half to a third as potent as, morphine. Following intramuscular administration it achieves effect in 15 minutes and maintains activity for three to six hours. The respiratory effects of nalbuphine resemble mor-

phine but, like butorphanol, there is a "ceiling" beyond which a further increase in dose does not increase the degree of depression. Cardiovascular effects differ from those of butorphanol, however, in that nalbuphine more nearly resembles morphine, having no significant impact in most patients on cardiac output or arterial, right atrial or pulmonary artery pressure. Nalbuphine has been given with favorable results to patients following myocardial infarction. The abuse potential of nalbuphine is judged low but is probably slightly greater than that of butorphanol.

The actions of both drugs are reversed by naloxone and they can precipitate withdrawal reactions in patients receiving long-term opiate therapy. At present they are not classified under the Controlled Substances Act. However, caution is advised—initially, meperidine and pentazocine were also thought to be nonaddicting. Butorphanol and nalbuphine should be treated like any potent parenteral mood-altering drug until time proves this unnecessary.

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Oxygen Monitoring

IN CLINICAL PRACTICE oxygen monitoring includes the sensing of gaseous oxygen in inspired and expired air, dissolved oxygen in arterial and venous blood, oxygen saturation in blood and tissue and whole body oxygen uptake. Rapidly progressing technology is providing monitoring instruments that are easier to use and less invasive.

Gaseous oxygen is monitored best by the polarographic technique. Four major manufacturers (Critikon, Instrumentation Laboratory, Teledyne and Beckman) produce such monitors, which cost between $300 and $600. The sensors, which are mounted directly in a patient's breathing circuit, have a life time of 3 to 12 months. These monitors, with direct readout and alarms, are considered standard equipment in many hospitals. More sophisticated monitors, including multiplexed mass spectrometers, paramagnetic sensors and heated fuel cells, are more accurate; however, because of their expense and size are used mainly as research tools.

Dissolved oxygen in arterial and venous blood is usually measured offline by bench instruments. New automated blood gas analyzers (Radiometer, Corning, Instrumentation Laboratory and Technicon) use microprocessors to perform automatic calibration, temperature compensation and simple calculations. Automated machines are two to three times more expensive than manual machines but they often replace a laboratory technician. A continuous monitor of dissolved oxygen is available from Critikon, but it has been designed for extracorporeal monitoring. Transcutaneous oxygen ($TcPo_2$) monitors, using heated Clark electrodes, provide information on arterial oxygen pressure (Pao_2) without the need for arterial puncture (Biochem, Radiometer, Litton, Novametrix and Roche). It must be realized that in adults, $TcPo_2$ is a measure of oxygen delivery and not Pao_2.

The oxygen saturation of arterial and venous blood can be measured offline with bench infrared (IR) instruments (Radiometer, Instrumentation Laboratory) or in vivo, using fiberoptic catheters (Physio-Control). The fiberoptic arterial and Swan-Ganz catheters are used to measure oxygen saturation by way of IR reflectance oximetry at the tip of a catheter. This method is invasive, the catheters are expensive ($50 to $70) and clot formation on the catheter tip can be a problem. Oxygen saturation can be monitored noninvasively using IR absorption through either the ear lobe or finger. (Hewlett-Packard and Corning) Because multiple wavelengths are needed to compensate for differences in skin pigmentation and movement artifacts, these instruments are cumbersome and expensive. Oxygen content, sometimes a more meaningful determination, is measured only offline (Cavitron).

The monitoring of oxygen at the tissue level is useful in detecting the shutdown of peripheral blood flow as an early indication of shock. Bare platinum wires have been used for monitoring in research studies but not for patient monitoring because of noise considerations. Solid state sensors and miniature polarographic sensors are being investigated.

Whole body oxygen consumption (Vo_2) is an indirect measure of a patient's metabolic requirements and may be used to monitor the incidence of shock. During administration of anesthesia, the Vo_2 may be related to depth of anesthesia. To monitor Vo_2 in the intensive care unit (ICU), mass spectrometer systems are multiplexed between several beds. Thus patients can share the